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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/492,028	01/26/2000	Charles S. Zuker	02307E- 092610	9361

20350 7590 06/15/2004

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/492,028	ZUKER, CHARLES S.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4 and 6-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 30 March 2004 has been entered in full. Claim 1 is amended and claims 3 and 8 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, and 6-7 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejections to claims 1, 3-4 and 6-8 under 35 U.S.C. § 112, first paragraph, as set forth at pg 2-6 of the previous Office Action (01 October 2003) are *withdrawn in part* in view of the cancelled claims and Applicant's persuasive arguments (30 March 2004). Please see section on 35 U.S.C. § 112, first paragraph below.

Specification

2. The objection to the specification regarding the issue of patent applications being referenced throughout the disclosure is maintained and held in abeyance until allowable subject matter is identified. This objection will be maintained until the referenced application (09/361,652) is abandoned or allowed or if the instant application is deemed allowable.

3. It is suggested that Applicant amend the instant specification to include the structural and functional features of the GPCR-B4 disclosed in application 09/361,631. Although it is permissible to incorporate essential matter into one specification by incorporating another U.S. Patent Application by reference, inclusion of this preferred embodiment in the instant specification would be in the public interest, should the instant application mature into a patent. The instant fact pattern is particularly confusing since the amino acid sequence of the preferred

embodiment only appears in the application which is incorporated by reference, and does not appear in the instant sequence listing. Introduction of new matter must be avoided.

Claim Rejections - 35 USC § 112, first paragraph

4. Claims 1, 4, and 6-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a compound that modulates signal transduction in taste cells, the method comprising the steps of: (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor comprising SEQ ID NOs: 1, 2, and 7 of 09/361, 631 with the compound, does not reasonably provide enablement for a method of identifying a compound that modulates signal transduction in taste cells, the method comprising the steps of: (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 2-6 of the previous Office Action of 01 October 2003 and at pg 3-8 of the Office Action of 12 February 2003.

Specifically, claims 1, 4 and 6-7 are directed to a method for identifying a compound that modulates signal transduction in taste cells, comprising the steps of (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide comprising a sequence of SEQ ID NO: 2, wherein the G-protein alpha subunit polypeptide is a subunit of a heterotrimeric G-protein which binds GTP and the G-protein alpha subunit polypeptide is

recombinantly expressed in the cell; and (ii) determining a functional effect of the compound upon the cell expressing the taste cell specific G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in taste cells. The claims also recite that the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G protein comprising the G-protein alpha subunit polypeptide. The claims recite that the G-protein alpha subunit polypeptide is from a mouse, rat, or human.

Applicant's arguments (30 March 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the specification offers guidance regarding the type of GPCR useful for the claimed screening methods (pg 11, lines 28-31).

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the specification of the instant application discloses that "although much is known about the psychophysics and physiology of taste cell function, very little is known about the molecules and pathways that mediate these sensory signaling responses" (pg 2, lines 30-33). The specification also teaches that "the identification and isolation of taste receptors (including taste ion channels), and taste signaling molecules, such as G-protein subunits and enzymes, involved in signal transduction, would allow for the pharmacological and genetic modulation of taste transduction pathways" (pg 3, lines 21-24). The state of the art at the time the instant application was filed indicates that no taste cell specific GPCR had been completely identified and characterized (Hoon et al., Cell 96: 541-551, 1999, pg 541, ¶ 5; Chandrashekar et al., Cell 100: 703-711, 2000, pg 709, 1st ¶ in col 1). However, USSN 09/361,631, now Patent No. 6,383,778, (incorporated by reference into the instant specification) discloses the polynucleotide

and polypeptide sequences of the taste cell specific G protein coupled receptor (GPCR), GPCR-B4. The specification also teaches that the GPCR-B4 receptor responds to the well-characterized bitter tastant, phenylthiocarbamide (PTC), but not to any of a number of natural or artificial sweeteners. However, the specifications of '631 and the instant application do not disclose all possible taste cell specific GPCRs. The skilled artisan would have to resort to trial and error experimentation to identify taste cell specific G protein coupled receptors, other than GPCR-B4.

According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis". The specification of the instant application does not disclose the specific identity of any other taste cell specific GPCRs other than GPCR-B4. This is not adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The skilled artisan still must resort to trial and error experimentation to identify and characterize a polypeptide as a cell specific GPCR. Such trial and error experimentation is considered undue.

It is noted to Applicant that the nucleic acid and amino acid sequences of *putative* taste cell specific GPCR termed GPCR-B3 have been identified in co-pending application, 09/361,652. However, this putative receptor has not been fully characterized. This putative taste cell specific GPCR has not demonstrated tissue and cell-specific expression, functional validation, or genetic corroboration (see Chandrashekar et al.; pg 709, 1st full ¶ in col 1).

Due to the large quantity of experimentation necessary to identify taste cell specific G protein coupled receptors and screen same for activity, the lack of direction/guidance directed to

the same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of identifying and characterizing, and the breadth of the claims which fail to recite any specific taste cell specific G protein coupled receptors, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

New 35 USC § 112, first paragraph, written description

5. Claims 1, 4 and 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method for identifying a compound that modulates signal transduction in taste cells, comprising the steps of (i) contacting a cell which expresses a taste cell specific G-protein alpha subunit polypeptide and a taste cell specific G protein coupled receptor with the compound, the G-protein alpha subunit polypeptide comprising a sequence of SEQ ID NO: 2, wherein the G-protein alpha subunit polypeptide is a subunit of a heterotrimeric G-protein which binds GTP and the G-protein alpha subunit polypeptide is recombinantly expressed in the cell; and (ii) determining a functional effect of the compound upon the cell expressing the taste cell specific G-protein alpha subunit polypeptide and the taste cell specific G protein coupled receptor, thereby identifying a compound that modulates signal transduction in taste cells. The claims also recite that the functional effect is determined by measuring increased or decreased binding of radiolabeled GTP to the G-protein alpha subunit polypeptide or to a G

protein comprising the G-protein alpha subunit polypeptide. The claims recite that the G-protein alpha subunit polypeptide is from a mouse, rat, or human.

The specification teaches the prophetic method wherein the taste cell specific G-protein alpha subunit polypeptide (TC-Gα14) is expressed in a heterologous cell with a taste cell specific G- protein coupled receptor such as GPCR-B3 or GPCR-B4 to screen for activators, inhibitors, and modulators of TC-Gα14 (pg 60, lines 1-11). The specification also discloses that the compounds tested as modulators can be any small chemical compound, or a biological entity, such as a protein, sugar, nucleic acid or lipid, the specification also teaches that "test compounds will be small chemical molecules and peptides...[and] essentially any chemical compound can be used as a potential modulator or ligand in the assays of the invention" (pg 33, lines 4-6). However, the specification does not teach compounds that modulate signal transduction in taste cells. The brief description in the specification of one taste cell specific GPCR (GPCR-B4; USSN 09/361,631 (Patent No. 6,383,778)) and one uncharacterized putative taste cell specific GPCR (GCPR-B3; USSN 09/361,652) is not adequate written description of an entire genus of taste cell specific G protein coupled receptors. Additionally, the description of one compound that modulates signal transduction (phenylthiocarbamide (PTC) (pg 56, line 29 of USSN 361,631 or col 40, line 46 of '778 patent) is not adequate written description of an entire genus of functionally equivalent compounds. It is noted that the Examiner was unable to find a list of tastant compounds disclosed in the specification of USSN 09/361,652. Also, the references Applicant relied upon for disclosure of tastant compounds in the Response of 30 March 2004 (e.g., Nelson 2001, Nelson 2002, and Chandrashekar 2000) were published after the filing date of the instant application. At the time of filing of the instant application, one skilled in the art would have resorted to trial and error experimentation to determine which class of compounds to

screen and which compounds have the desired activity recited in the claims. Furthermore, even if the references had been published before the filing date of the instant application, the specification does not teach the specific compounds that are disclosed in the cited references.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the taste cell specific G protein coupled receptors or compounds of the encompassed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The detectable signal or signaling pathway itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

Therefore, only a specific taste cell specific G protein coupled receptor (GPCR-B4) and a specific compound(s), but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear

that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure (chemosensory receptors):

Matsunami et al. Nature 404 : 601-604, 2000.

Mombaerts, P. Science 286 : 707-711, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
09 June 2004

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